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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,705	02/06/2001	Karl Guegler	CLO01010	5353

25748 7590 08/25/2003

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	19

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,705	GUEGLER ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,8,9,13 and 24-28* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,8,9 and 24-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *4,8,9,13 and 24-28* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14,17*.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 12 June 2003 (Paper No. 16) has been entered in full. Claims 4, 24-25, and 27-28 are amended.

This application contains claim 13 drawn to an invention nonelected with traverse in Paper No. 12 (11 November 2002). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 4, 8-9, and 24-28 are under consideration in the instant application.

Sequence Compliance

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 16, 12 June 2003) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (Paper No. 13, 12 February 2003) are withdrawn.

Withdrawn Objections and/or Rejections

1. The objections to the specification at pg 3-43of the previous Office Action (Paper No. 13, 12 February 2003) are *withdrawn* in view of the amended specification and title (Paper No. 16, 12 June 2003).

2. The rejections to claims 24-25 and 27-28 under 35 U.S.C. § 112, second paragraph as set forth at pg 9-10 of the previous Office Action (Paper No. 13, 12 November 2002) are *withdrawn*

in part in view of the amended claims (Paper No. 16, 12 June 2003). Please see section on 35 U.S.C. § 112, second paragraph, below.

Information Disclosure Statement

3. The supplemental information disclosure statements filed on 21 February 2003 (Paper No. 14) and 12 June 2003 (Paper No. 17) have been considered. It is noted to Applicant that Hatanaka et al. (2001) and Sugawara et al. (2000) had been previously considered by the Examiner (see PTO-892 of 12 November 2002) and therefore, have been crossed off the IDS of 21 February 2003 (Paper No. 14). However, Gu et al. (2001) has not been considered by the Examiner because no copy of that publication was received.

Drawings

4. The formal drawings filed on 12 June 2003 (Paper No. 17) have been considered by the Examiner.

Claim Objections

5. Claim 4 is objected to because of the following informalities:

5a. Claim 4 does not recite the claimed polynucleotides as a proper Markush group. The word "and" is missing after 4(b) and before 4(c).

5b. In claim 4(b), the word "the" should be deleted.

5c. In claim 4(b), the word "No" should be completely capitalized.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and § 112, first paragraph

6. Claims 4, 8-9, and 24-28 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established

utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. The basis for this rejection is set forth at pg 4-9 of the previous Office Action (Paper No. 13, 12 February 2003).

5. Claims 4, 8-9 and 24-28 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Specifically, claims 4, 8-9, and 24-28 are directed to an isolated nucleic acid molecule consisting of a nucleotide sequence consisting of (a) a nucleotide sequence that encodes a protein comprising the amino acid sequence of SEQ ID NO: 2, (b) a nucleotide sequence consisting of SEQ ID NO: 1, and (c) a nucleotide sequence that is completely complementary to a nucleotide sequence of (a)-(b). The claims also recite a vector, host cell, and a process for producing a polypeptide.

Applicant's arguments (Paper No. 16, 12 May 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts Applicant asserts at page 8 of the Response (Paper No. 14, 22 July 2002), that the claimed isolated nucleic acid molecules, such as SEQ ID NOs: 1 and 3, that encode a specified amino acid sequence, SEQ ID NO: 2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 USC § 101 and the first paragraph of 35 USC §112. Applicant argues that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, and therefore have utility. Applicant

submits that the isolated nucleic acid molecules of the present invention, which encode a novel transporter protein of SEQ ID NO: 2 (specifically, a transporter family protein), has utility in the drug discovery process. Applicant contends that the nucleic acid molecules and polypeptides of the instant application provide sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. Applicant also asserts that the nucleic acid molecules and polypeptides of the instant application have commercial utilities, such as screening potential drug compounds, producing antibodies, developing hybridization probes and primers, tissue markers, or treating diseases affecting whole embryo, hepatocellular carcinoma, non-cancerous liver, fetal liver spleen and liver. It is noted that Applicant cites *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980); *Juicy Whip v. Orange Bang Inc.*, 51 USPQ2d 1700.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, the polynucleotides (SEQ ID NOs: 1 and 3) and polypeptide (SEQ ID NO: 2) of the instant application are not supported by either a credible, specific and substantial ("real-world") asserted utility or a well established utility. The claimed transporter polynucleotides and polypeptide do not have a substantial utility because basic research is required to study the properties and activity of the claimed polynucleotide that encodes polypeptide. The specification of the instant application does not disclose the function of the transporter polynucleotide and polypeptide and only recites prophetic examples of how the claimed polynucleotide and polypeptide can be utilized in various assays (pg 42-53). Commercial success is not necessarily evidence of patentable utility. Commercial success requires more than the mere sale of a compound and sale of a compound for use as a scientific tool does not appear to be a specific,

substantial and credible utility as set forth in the "REVISED INTERIM UTILITY GUIDELINES". Commercial success is discussed in the MPEP at 716.03 and appears to be applicable to obviousness rejections, but does not appear to be a valid consideration for utility which requires specific, substantial and credible utility. Applicant also has not established a nexus between the *claimed* invention and evidence of commercial success. Furthermore, the fact patterns of the cases cited by the Applicant (*Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980); *Juicy Whip v. Orange Bang Inc.*, 51 USPQ2d 1700) and of the instant rejection are significantly different, and the court decisions are not binding with regard to the instant rejections.

(ii) Applicant asserts that the specification and figures show that the protein of the present invention has a functional domain of a transporter. Applicant argues that sufficient disclosure of functional characteristics and biological roles of the transporter polypeptide of SEQ ID NO: 2 and encoding polynucleotides (SEQ ID NOs: 1 and 3) are provided such that undue experimentation would not be required by any one of ordinary skill in the art to know how to use the claimed invention. Applicant states that there is overwhelming evidence in the art to support the utility of novel transporter proteins and encoding nucleic acid molecules, particularly those related to the amino acid transport system A (ATA) family. Applicant also contends the uses are quite specific for the transporter family of proteins, even though each member may play a different role in cellular responses and pathologies. Applicant submits that even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific, and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

Applicant's arguments have been fully considered but are not found to be persuasive. Although Applicant asserts the claimed nucleic acid molecules (SEQ ID NOs: 1 and 3) are homologous to existing transporters, particularly the amino acid transport system A (ATA) family, Palacin et al. (Physiol Rev 78(4): 969-1054, 1998) teach that a particular transport system carries different amino acids and that amino acid transport systems show overlapping specificities (pg 970, ¶ 3). Palacin et al. also indicate that the system A transport system is highly regulated (including upregulation during cell-cycle progression, cell growth, and hormonal control) and the lack of structural information on the system A transporter prevents further understanding the molecular mechanisms underlying system A regulation (pg 971, col 1-2 through pg 972, lines 1-4; pg 973-975). Palacin et al. disclose that the functional classification of amino acid transporters has been retained since the structural information of higher eukaryote amino acid transporters is incomplete (pg 969, col 2 to pg 970, lines 1-2). Additionally, the specification of the instant application does not teach the skilled artisan which domains of the claimed nucleic acid molecules of SEQ ID NOs: 1 and 3 are characteristic of transporters, specifically system A amino acid transporters. The specification also does not teach any methods or working examples to demonstrate that the polypeptide of SEQ ID NO: 2 of the instant application has any functional activity. One skilled in the art would not know the utility and function of the polypeptide in the instant specification, even if it was a putative system A amino acid transporter because, as discussed in the related art above and the specification of the instant application, system A amino acid transporters (and transporters in general) regulate many different functions of a cell.

Although Applicant asserts that one of skill in the art would recognize the claimed polynucleotides as system A amino acid transporters based on homology to other transporters, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in sequence databases. Skolnick et al. (Trends in Biotech 18:34-39, 2000) states that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (Box 2, pg 36 Skolnick). Additionally, the problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. Certain positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions. Furthermore, as indicated above, amino acid transporters are classified according to function since the structural information of higher eukaryote amino acid transporters is incomplete (Palacin et al., pg 969, col 2 to pg 970, lines 1-2).

It is clear from the instant specification that the polypeptide of SEQ ID NO: 2 described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this DNA and protein, may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966),

in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

(iii) Applicant asserts that the discloses uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediate is sufficient to satisfy the requirements of 35 U.S.C. § 101 and § 112, first paragraph (see pg 11 of Response). Applicant also argues that exemplary uses of the nucleic acid sequence are recited in the specification on pages 43-63. Applicant argues that among the examples, the nucleic acid molecules are useful as hybridization probes for mRNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. Applicant adds that an expression vector comprising the nucleic acid sequences can be made that express the transporter protein. Applicant contends that such uses are specific for claimed nucleic acid molecules, and the products of such uses will be clearly different than what would be produced using a different nucleic acid molecule for the same purpose. Applicant also indicates that the

present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function.

Applicant's arguments have been fully considered but are not found to be persuasive. It is noted to Applicant that the Examiner has previously reviewed why the asserted patentable utilities for the claimed putative polynucleotide (SEQ ID NO: 1 or 3) listed in the specification are not credible, specific and substantial asserted utilities (see pages 5-9 of the previous Office Action, 12 November 2002, Paper No. 13). The asserted utility of using the claimed nucleic acid molecules as hybridization probes is credible but not substantial or specific. Hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial. The asserted utility of producing protein targets for the identifying agents that bind to the protein targets and modulate protein function is not specific or substantial. Such assays can be performed with any polynucleotide and polypeptide. Further, the specification discloses nothing specific or substantial for the protein targets and other agents that can be identified by this method.. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

Therefore, the regulation and sequestration of the particular polynucleotides and polypeptide of the instant application, is not well characterized and one skilled in the art the art would not find the utility of the claimed polynucleotides to be obvious.

35 USC § 112, second paragraph

7. Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 24 is rejected as being indefinite because the claims recite a recombinant method for producing a polypeptide comprising insertion of the polynucleotide of claim 4 into a host cell. Claim 4(d) recites a polynucleotide consisting of "a nucleotide sequence that is completely complementary to a nucleotide sequence of (a)-(c)". It is not clear how the polynucleotide complements of claim 4(d) produce the polypeptide disclosed in the instant application. A complement is a sequence of nucleotide bases in one strand of a DNA or RNA molecule that is exactly complementary (adenine-thymine, adenine-uracil, or guanine-cytosine) to that on another single strand.

Applicant's arguments (Paper No. 16, 12 May 2003), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that claim 4 has been amended to specifically recite "a nucleic acid molecule that encodes said polypeptide". Applicant adds that the polypeptide is SEQ ID NO: 2. Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, as indicated in the previous Office Action (pg 10), a complement is a sequence of nucleotide bases in one strand of a DNA or RNA molecule that is exactly complementary (adenine-thymine, adenine-uracil, or guanine-cytosine) to that on another single strand. Therefore, it is still not clear to the Examiner how polynucleotide complements produce the

polypeptide of SEQ ID NO: 2. The recitation of the phrase "a nucleic acid molecule that encodes said polypeptide" does not overcome this issue.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
August 11, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER